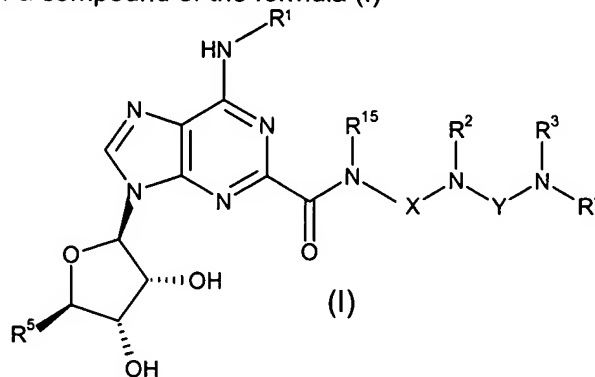


- Amendments to the Claims -

1. - 57. (Canceled)

58. (Currently amended) A method of treatment of a mammal, including a human being, to treat an inflammatory disease including treating said mammal with an effective amount of a compound of the formula (I)



or a pharmaceutically acceptable salt or solvate thereof, wherein  
R<sup>1</sup> is H, C<sub>1</sub>-C<sub>6</sub> alkyl or fluorenyl, said C<sub>1</sub>-C<sub>6</sub> alkyl being optionally substituted by 1 or 2 substituents each independently selected from phenyl and naphthyl, said phenyl and naphthyl being optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, halo or cyano;  
(A) R<sup>2</sup> is H or C<sub>1</sub>-C<sub>6</sub> alkyl, R<sup>15</sup> is H or C<sub>1</sub>-C<sub>6</sub> alkyl, and X is either (i) unbranched C<sub>2</sub>-C<sub>3</sub> alkylene optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl or C<sub>3</sub>-C<sub>8</sub> cycloalkyl, or (ii) a group of the formula:



where W is C<sub>5</sub>-C<sub>7</sub> cycloalkylene optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl, n is 0 or 1 and p is 0 or 1, or

(B) R<sup>15</sup> is H or C<sub>1</sub>-C<sub>6</sub> alkyl, and R<sup>2</sup> and X, taken together with the nitrogen atom to which they are attached, represent azetidin-3-yl, pyrrolidin-3-yl, piperidin-3-yl, piperidin-4-yl, homopiperidin-3-yl or homopiperidin-4-yl, each being optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl, or

(C) R<sup>2</sup> is H or C<sub>1</sub>-C<sub>6</sub> alkyl, and R<sup>15</sup> and X, taken together with the nitrogen atom to which they are attached, represent azetidin-3-yl, pyrrolidin-3-yl, piperidin-3-yl, piperidin-4-yl, homopiperidin-3-yl or homopiperidin-4-yl, each being optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl;

either, R<sup>3</sup> and R<sup>4</sup>, taken together with the nitrogen atom to which they are attached, represent azetidiny, pyrrolidinyl, piperidinyl, piperazinyl, homopiperidinyl or homopiperazinyl, each being optionally substituted on a ring nitrogen or carbon atom by C<sub>1</sub>-C<sub>6</sub> alkyl or C<sub>3</sub>-C<sub>8</sub> cycloalkyl and optionally substituted on a ring carbon atom not adjacent to a ring nitrogen atom by -NR<sup>6</sup>R<sup>7</sup>,

or, R<sup>3</sup> is H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl or benzyl and R<sup>4</sup> is

(a) azetidin-3-yl, pyrrolidin-3-yl, piperidin-3-yl, piperidin-4-yl, homopiperidin-3-yl or homopiperidin-4-yl, each being optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, phenyl, benzyl or het, or

(b) -(C<sub>2</sub>-C<sub>6</sub> alkylene)-R<sup>8</sup>

(c) -(C<sub>1</sub>-C<sub>6</sub> alkylene)-R<sup>13</sup>, or

(d) C<sub>1</sub>-C<sub>6</sub> alkyl or C<sub>3</sub>-C<sub>8</sub> cycloalkyl;

R<sup>5</sup> is CH<sub>2</sub>OH or CONR<sup>14</sup>R<sup>14</sup>;

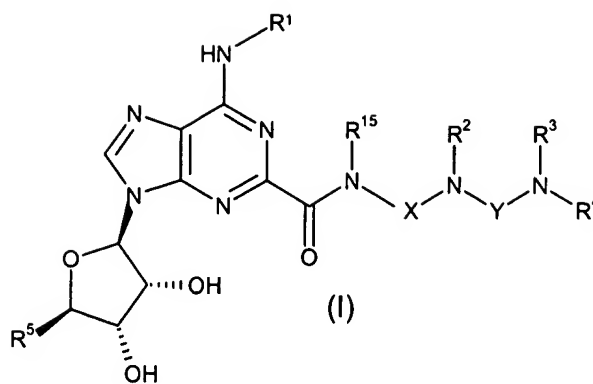
R<sup>6</sup> and R<sup>7</sup> are either each independently H or C<sub>1</sub>-C<sub>6</sub> alkyl or, taken together with the nitrogen atom to which they are attached, represent azetidiny, pyrrolidinyl or

piperidinyl, said azetidiny, pyrrolidinyl and piperidinyl being optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl;  
R<sup>8</sup> is (i) azetidin-1-yl, pyrrolidin-1-yl, piperidin-1-yl, morpholin-4-yl, piperazin-1-yl, homopiperidin-1-yl, homopiperazin-1-yl or tetrahydroisoquinolin-1-yl, each being optionally substituted on a ring carbon atom by C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, phenyl, C<sub>1</sub>-C<sub>6</sub> alkoxy-(C<sub>1</sub>-C<sub>6</sub>)-alkyl, R<sup>9</sup>R<sup>9</sup>N-(C<sub>1</sub>-C<sub>6</sub>)-alkyl, fluoro-(C<sub>1</sub>-C<sub>6</sub>)-alkyl, -CONR<sup>9</sup>R<sup>9</sup>, -COOR<sup>9</sup> or C<sub>2</sub>-C<sub>5</sub> alkanoyl, and optionally substituted on a ring carbon atom not adjacent to a ring nitrogen atom by fluoro-(C<sub>1</sub>-C<sub>6</sub>)-alkoxy, halo, -OR<sup>9</sup>, cyano, -S(O)<sub>m</sub>R<sup>10</sup>, -NR<sup>9</sup>R<sup>9</sup>, -SO<sub>2</sub>NR<sup>9</sup>R<sup>9</sup>, -NR<sup>9</sup>COR<sup>10</sup> or -NR<sup>9</sup>SO<sub>2</sub>R<sup>10</sup>, and said piperazin-1-yl and homopiperazin-1-yl being optionally substituted on the ring nitrogen atom not attached to the C<sub>2</sub>-C<sub>6</sub> alkylene group by C<sub>1</sub>-C<sub>6</sub> alkyl, phenyl, C<sub>1</sub>-C<sub>6</sub> alkoxy-(C<sub>2</sub>-C<sub>6</sub>)-alkyl, R<sup>9</sup>R<sup>9</sup>N-(C<sub>2</sub>-C<sub>6</sub>)-alkyl, fluoro-(C<sub>1</sub>-C<sub>6</sub>)-alkyl, C<sub>2</sub>-C<sub>5</sub> alkanoyl, -COOR<sup>10</sup>, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, -SO<sub>2</sub>R<sup>10</sup>, -SO<sub>2</sub>NR<sup>9</sup>R<sup>9</sup> or -CONR<sup>9</sup>R<sup>9</sup>, or  
(ii) NR<sup>11</sup>R<sup>12</sup>;  
R<sup>9</sup> is H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl or phenyl;  
R<sup>10</sup> is C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl or phenyl;  
R<sup>11</sup> is H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl or benzyl;  
R<sup>12</sup> is H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, phenyl, benzyl, fluoro-(C<sub>1</sub>-C<sub>6</sub>)-alkyl, -CONR<sup>9</sup>R<sup>9</sup>, -COOR<sup>10</sup>, C<sub>2</sub>-C<sub>5</sub> alkanoyl or -SO<sub>2</sub>NR<sup>9</sup>R<sup>9</sup>;  
R<sup>13</sup> is (a) phenyl, pyridin-2-yl, pyridin-3-yl or pyridin-4-yl, each being optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, -(C<sub>1</sub>-C<sub>3</sub> alkylene)-(C<sub>1</sub>-C<sub>6</sub> alkoxy), halo, cyano, -(C<sub>1</sub>-C<sub>3</sub> alkylene)-CN, -CO<sub>2</sub>H, -(C<sub>1</sub>-C<sub>3</sub> alkylene)-CO<sub>2</sub>H, -CO<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), -(C<sub>1</sub>-C<sub>3</sub> alkylene)-CO<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), -(C<sub>1</sub>-C<sub>3</sub> alkylene)-NR<sup>14</sup>R<sup>14</sup>, -CONR<sup>14</sup>R<sup>14</sup> or -(C<sub>1</sub>-C<sub>3</sub> alkylene)-CONR<sup>14</sup>R<sup>14</sup>, or (b) azetidin-2-yl, azetidin-3-yl, pyrrolidin-2-yl, pyrrolidin-3-yl, piperidin-2-yl, piperidin-3-yl, piperidin-4-yl, homopiperidin-2-yl, homopiperidin-3-yl or homopiperidin-4-yl, each being optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, phenyl, benzyl or het;  
R<sup>14</sup> is H or C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted by cyclopropyl;  
m is 0, 1 or 2;  
Y is CO, CS, SO<sub>2</sub> or C=N(CN); and  
"het", used in the definition of R<sup>4</sup> and R<sup>13</sup>, is a C-linked, 4- to 6-membered ring, heterocycle having either from 1 to 4 ring nitrogen heteroatoms or 1 or 2 nitrogen ring heteroatoms and 1 oxygen or 1 sulphur ring heteroatom, optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>3</sub>-C<sub>8</sub> cycloalkoxy, hydroxy, oxo or halo or with a pharmaceutically acceptable salt, solvate or composition thereof, as claimed in any one of claims 1 to 44 and 45 respectively.

59. (Canceled)

60. (Canceled)

61. (Original) A method of treatment of a mammal, including a human being, to treat septic shock, male erectile dysfunction, male factor infertility, female factor infertility, hypertension, stroke, epilepsy, cerebral ischaemia, peripheral vascular disease, post-ischaemic reperfusion injury, diabetes, rheumatoid arthritis, multiple sclerosis, psoriasis, dermatitis, allergic dermatitis, eczema, ulcerative colitis, Crohns disease, inflammatory bowel disease, *Helicobacter pylori* gastritis, non-*Helicobacter pylori* gastritis, non-steroidal anti-inflammatory drug-induced damage to the gastrointestinal tract or a psychotic disorder, or for wound healing, including treating said mammal with an effective amount of a compound of the formula (I)



or a pharmaceutically acceptable salt or solvate thereof, wherein

$R^1$  is H,  $C_1$ - $C_6$  alkyl or fluorenyl, said  $C_1$ - $C_6$  alkyl being optionally substituted by 1 or 2 substituents each independently selected from phenyl and naphthyl, said phenyl and naphthyl being optionally substituted by  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy, halo or cyano;

(A)  $R^2$  is H or  $C_1$ - $C_6$  alkyl,  $R^{15}$  is H or  $C_1$ - $C_6$  alkyl, and X is either (i) unbranched  $C_2$ - $C_3$  alkylene optionally substituted by  $C_1$ - $C_6$  alkyl or  $C_3$ - $C_8$  cycloalkyl, or (ii) a group of the formula:



where W is  $C_5$ - $C_7$  cycloalkylene optionally substituted by  $C_1$ - $C_6$  alkyl, n is 0 or 1 and p is 0 or 1, or

(B)  $R^{15}$  is H or  $C_1$ - $C_6$  alkyl, and  $R^2$  and X, taken together with the nitrogen atom to which they are attached, represent azetidin-3-yl, pyrrolidin-3-yl, piperidin-3-yl, piperidin-4-yl, homopiperidin-3-yl or homopiperidin-4-yl, each being optionally substituted by  $C_1$ - $C_6$  alkyl, or

(C)  $R^2$  is H or  $C_1$ - $C_6$  alkyl, and  $R^{15}$  and X, taken together with the nitrogen atom to which they are attached, represent azetidin-3-yl, pyrrolidin-3-yl, piperidin-3-yl, piperidin-4-yl, homopiperidin-3-yl or homopiperidin-4-yl, each being optionally substituted by  $C_1$ - $C_6$  alkyl;

either,  $R^3$  and  $R^4$ , taken together with the nitrogen atom to which they are attached, represent azetidiny, pyrrolidinyl, piperidinyl, piperazinyl, homopiperidinyl or homopiperazinyl, each being optionally substituted on a ring nitrogen or carbon atom by  $C_1$ - $C_6$  alkyl or  $C_3$ - $C_8$  cycloalkyl and optionally substituted on a ring carbon atom not adjacent to a ring nitrogen atom by  $-NR^6R^7$ ,

or,  $R^3$  is H,  $C_1$ - $C_6$  alkyl,  $C_3$ - $C_8$  cycloalkyl or benzyl and  $R^4$  is

(a) azetidin-3-yl, pyrrolidin-3-yl, piperidin-3-yl, piperidin-4-yl, homopiperidin-3-yl or homopiperidin-4-yl, each being optionally substituted by  $C_1$ - $C_6$  alkyl,  $C_3$ - $C_8$  cycloalkyl, phenyl, benzyl or het, or

(b)  $-(C_2-C_6 \text{ alkylene})-R^8$

(c)  $-(C_1-C_6 \text{ alkylene})-R^{13}$ , or

(d)  $C_1$ - $C_6$  alkyl or  $C_3$ - $C_8$  cycloalkyl;

$R^9$  is  $CH_2OH$  or  $CONR^{14}R^{14}$ ;

$R^6$  and  $R^7$  are either each independently H or  $C_1$ - $C_6$  alkyl or, taken together with the nitrogen atom to which they are attached, represent azetidiny, pyrrolidinyl or piperidinyl, said azetidiny, pyrrolidinyl and piperidinyl being optionally substituted by  $C_1$ - $C_6$  alkyl;

$R^8$  is (i) azetidin-1-yl, pyrrolidin-1-yl, piperidin-1-yl, morpholin-4-yl, piperazin-1-yl, homopiperidin-1-yl, homopiperazin-1-yl or tetrahydroisoquinolin-1-yl, each being optionally substituted on a ring carbon atom by  $C_1$ - $C_6$  alkyl,  $C_3$ - $C_8$  cycloalkyl, phenyl,  $C_1$ - $C_6$  alkoxy- $(C_1-C_6)$ -alkyl,  $R^9R^9N-(C_1-C_6)$ -alkyl, fluoro- $(C_1-C_6)$ -alkyl,  $-CONR^9R^9$ ,  $-COOR^9$  or  $C_2$ - $C_5$  alkanoyl, and optionally substituted on a ring carbon atom not adjacent to a ring nitrogen atom by fluoro- $(C_1-C_6)$ -alkoxy, halo,  $-OR^9$ , cyano,  $-S(O)_mR^{10}$ ,

-NR<sup>9</sup>R<sup>9</sup>, -SO<sub>2</sub>NR<sup>9</sup>R<sup>9</sup>, -NR<sup>9</sup>COR<sup>10</sup> or -NR<sup>9</sup>SO<sub>2</sub>R<sup>10</sup>, and said piperazin-1-yl and homopiperazin-1-yl being optionally substituted on the ring nitrogen atom not attached to the C<sub>2</sub>-C<sub>6</sub> alkylene group by C<sub>1</sub>-C<sub>6</sub> alkyl, phenyl, C<sub>1</sub>-C<sub>6</sub> alkoxy-(C<sub>2</sub>-C<sub>6</sub>)-alkyl, R<sup>9</sup>R<sup>9</sup>N-(C<sub>2</sub>-C<sub>6</sub>)-alkyl, fluoro-(C<sub>1</sub>-C<sub>6</sub>)-alkyl, C<sub>2</sub>-C<sub>5</sub> alkanoyl, -COOR<sup>10</sup>, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, -SO<sub>2</sub>R<sup>10</sup>, -SO<sub>2</sub>NR<sup>9</sup>R<sup>9</sup> or -CONR<sup>9</sup>R<sup>9</sup>, or

(ii) NR<sup>11</sup>R<sup>12</sup>,

R<sup>9</sup> is H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl or phenyl;

R<sup>10</sup> is C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl or phenyl;

R<sup>11</sup> is H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl or benzyl;

R<sup>12</sup> is H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, phenyl, benzyl, fluoro-(C<sub>1</sub>-C<sub>6</sub>)-alkyl, -CONR<sup>9</sup>R<sup>9</sup>, -COOR<sup>10</sup>, C<sub>2</sub>-C<sub>5</sub> alkanoyl or -SO<sub>2</sub>NR<sup>9</sup>R<sup>9</sup>;

R<sup>13</sup> is (a) phenyl, pyridin-2-yl, pyridin-3-yl or pyridin-4-yl, each being optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, -(C<sub>1</sub>-C<sub>3</sub> alkylene)-(C<sub>1</sub>-C<sub>6</sub> alkoxy), halo, cyano, -(C<sub>1</sub>-C<sub>3</sub> alkylene)-CN, -CO<sub>2</sub>H, -(C<sub>1</sub>-C<sub>3</sub> alkylene)-CO<sub>2</sub>H, -CO<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), -(C<sub>1</sub>-C<sub>3</sub> alkylene)-CO<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), -(C<sub>1</sub>-C<sub>3</sub> alkylene)-NR<sup>14</sup>R<sup>14</sup>, -CONR<sup>14</sup>R<sup>14</sup> or -(C<sub>1</sub>-C<sub>3</sub> alkylene)-CONR<sup>14</sup>R<sup>14</sup>, or (b) azetidin-2-yl, azetidin-3-yl, pyrrolidin-2-yl, pyrrolidin-3-yl, piperidin-2-yl, piperidin-3-yl, piperidin-4-yl, homopiperidin-2-yl, homopiperidin-3-yl or homopiperidin-4-yl, each being optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, phenyl, benzyl or het;

R<sup>14</sup> is H or C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted by cyclopropyl;

m is 0, 1 or 2;

Y is CO, CS, SO<sub>2</sub> or C=N(CN); and

"het", used in the definition of R<sup>4</sup> and R<sup>13</sup>, is a C-linked, 4- to 6-membered ring, heterocycle having either from 1 to 4 ring nitrogen heteroatoms or 1 or 2 nitrogen ring heteroatoms and 1 oxygen or 1 sulphur ring heteroatom, optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>3</sub>-C<sub>8</sub> cycloalkoxy, hydroxy, oxo or halo or with a pharmaceutically acceptable salt, solvate or composition thereof, as claimed in any one of claims 1 to 44 and 45 respectively.

62. - 77. (Canceled)

An early and favorable action is respectfully requested.

Respectfully submitted,

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